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ELSEVIER FULL-TEXT ARTICLE

Hypervariable region 1 of hepatitis C virus: immunological decoy or biologically relevant domain?

Mondelli MU, Cerino A, Segagni L, Meola A, Cividini A, Silini E, Nicosia A.

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The hypervariable region 1 (HVR1) of the E2 protein of hepatitis C virus (HCV) is highly heterogeneous and is responsible for significant inter- and intra-individual variation of the infecting virus, which may represent an important pathogenetic mechanism leading to escape and persistent infection. Moreover, a binding site for neutralizing antibodies (Ab) has been allegedly identified in this region. Prospective studies of serological responses to synthetic oligopeptides derived from HVR1 sequences of patients with acute and chronic HCV infection showed extensive serological cross-reactivity for unrelated HVR1 peptides in the majority of the patients. A significant correlation was found between HVR1 sequence variation, and intensity, and cross-reactivity of humoral immune responses providing strong evidence in support of the contention that HCV variant selection is driven by the host immune pressure. Monoclonal Ab (mAb) generated following immunization of mice with peptides derived from natural HVR1 sequences also showed cross-reactivity for several HVR1 sequences attesting to the existence of conserved amino acid motifs among different variants. These findings suggest that it is possible to induce a broadly cross-reactive immune response to HVR1 and that this mechanism can be used to generate protective immunity for a large repertoire of HCV variants.

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